FIGURE 1

TRRYYLGAVELSW,	RRYYLGAVELSWD,	RYYLGAVELSWDY,	YYLGAVELSWDYM,
GAVELSWDYMQSD,	VELSWDYMQSDLG,	LSWDYMQSDLGEL,	WDYMQSDLGELPV,
DYMQSDLGELPVD,	SDLGELPVDARFP,	GELPVDARFPPRV,	LPVDARFPPRVPK,
ARFPPRVPKSFPF,	PRVPKSFPFNTSV,	PKSFPFNTSVVYK,	KSFPFNTSVVYKK,
FPFNTSVVYKKTL,	TSVVYKKTLFVEF,	SVVYKKTLFVEFT,	VVYKKTLFVEFTD,
KTLFVEFTDHLFN,	TLFVEFTDHLFNI,	LFVEFTDHLFNIA,	VEFTDHLFNIAKP,
EFTDHLFNIAKPR,	DHLFNIAKPRPPW,	HLFNIAKPRPPWM,	FNIAKPRPPWMGL,
PPWMGLLGPTIQA,	PWMGLLGPTIQAE,	MGLLGPTIQAEVY,	GLLGPTIQAEVYD,
LLGPTIQAEVYDT,	PTIQAEVYDTVVI,	AEVYDTVVITLKN,	EVYDTVVITLKNM,
VYDTVVITLKNMA,	DTVVITLKNMASH,	TVVITLKNMASHP,	VVITLKNMASHPV,
ITLKNMASHPVSL,	TLKNMASHPVSLH,	KNMASHPVSLHAV,	SHPVSLHAVGVSY,
HPVSLHAVGVSYW,	PVSLHAVGVSYWK,	VSLHAVGVSYWKA,	HAVGVSYWKASEG,
VGVSYWKASEGAE,	VSYWKASEGAEYD,	SYWKASEGAEYDD,	EGAEYDDQTSQRE,
AEYDDQTSQREKE,	QREKEDDKVFPGG,	DKVFPGGSHTYVW,	KVFPGGSHTYVWQ,
GSHTYVWQVLKEN,	HTYVWQVLKENGP,	TYVWQVLKENGPM,	YVWQVLKENGPMA,
WQVLKENGPMASD,	QVLKENGPMASDP,	KENGPMASDPLCL,	GPMASDPLCLTYS,
DPLCLTYSYLSHV,	LCLTYSYLSHVDL,	LTYSYLSHVDLVK,	YSYLSHVDLVKDL,
SYLSHVDLVKDLN,	SHVDLVKDLNSGL,	VDLVKDLNSGLIG,	DLVKDLNSGLIGA,
KDLNSGLIGALLV,	DLNSGLIGALLVC,	LNSGLIGALLVCR,	SGLIGALLVCREG,
GLIGALLVCREGS,	IGALLVCREGSLA,	GALLVCREGSLAK,	ALLVCREGSLAKE,
LLVCREGSLAKEK,	GSLAKEKTQTLHK,	QTLHKFILLFAVF,	TLHKFILLFAVFD,
HKFILLFAVFDEG,	KFILLFAVFDEGK,	FILLFAVFDEGKS,	ILLFAVFDEGKSW,
LLFAVFDEGKSWH,	FAVFDEGKSWHSE,	AVFDEGKSWHSET,	KSWHSETKNSLMQ,
NSLMQDRDAASAR,	SLMQDRDAASARA,	MQDRDAASARAWP,	RAWPKMHTVNGYV,
PKMHTVNGYVNRS,	HTVNGYVNRSLPG,	NGYVNRSLPGLIG,	GYVNRSLPGLIGC,
RSLPGLIGCHRKS,	PGLIGCHRKSVYW,	GLIGCHRKSVYWH,	KSVYWHVIGMGTT,
SVYWHVIGMGTTP,	VYWHVIGMGTTPE,	WHVIGMGTTPEVH,	HVIGMGTTPEVHS,
IGMGTTPEVHSIF,	GTTPEVHSIFLEG,	PEVHSIFLEGHTF,	HSIFLEGHTFLVR,
SIFLEGHTFLVRN,	IFLEGHTFLVRNH,	GHTFLVRNHRQAS,	HTFLVRNHRQASL,
TFLVRNHRQASLE,	FLVRNHRQASLEI,	VRNHRQASLEISP,	RQASLEISPITFL,
QASLEISPITFLT,	ASLEISPITFLTA,	LEISPITFLTAQT,	ISPITFLTAQTLL,
SPITFLTAQTLLM,	ITFLTAQTLLMDL,	TFLTAQTLLMDLG,	QTLLMDLGQFLLF,
TLLMDLGQFLLFC,	LLMDLGQFLLFCH,	MDLGQFLLFCHIS,	DLGQFLLFCHISS,
GQFLLFCHISSHQ,	QFLLFCHISSHQH,	FLLFCHISSHQHD,	LLFCHISSHQHDG,
CHISSHQHDGMEA,	SSHQHDGMEAYVK,	DGMEAYVKVDSCP,	EAYVKVDSCPEEP,
AYVKVDSCPEEPQ,	VKVDSCPEEPQLR,	DSCPEEPQLRMKN,	PQLRMKNNEEAED,
LRMKNNEEAEDYD,	NEEAEDYDDDLTD,	EDYDDDLTDSEMD,	DDDLTDSEMDVVR,
DDLTDSEMDVVRF,	SEMDVVRFDDDNS,	MDVVRFDDDNSPS,	DVVRFDDDNSPSF,
VVRFDDDNSPSFI,	VRFDDDNSPSFIQ,	DNSPSFIQIRSVA,	PSFIQIRSVAKKH,
SFIQIRSVAKKHP,	IQIRSVAKKHPKT,	RSVAKKHPKTWVH,	KTWVHYIAAEEED,
TWVHYIAAEEEDW,	VHYIAAEEEDWDY,	HYIAAEEEDWDYA,	EDWDYAPLVLAPD,
WDYAPLVLAPDDR,	APLVLAPDDRSYK,	PLVLAPDDRSYKS,	LVLAPDDRSYKSQ,
VLAPDDRSYKSQY,	RSYKSQYLNNGPQ,	YKSQYLNNGPQRI,	SQYLNNGPQRIGR,
QYLNNGPQRIGRK,	NGPQRIGRKYKKV,	QRIGRKYKKVRFM,	RKYKKVRFMAYTD,
KKVRFMAYTDETF,	KVRFMAYTDETFK,	VRFMAYTDETFKT,	RFMAYTDETFKTR,
FMAYTDETFKTRE,	MAYTDETFKTREA,	YTDETFKTREAIQ,	ETFKTREAIQHES,
FKTREAIQHESGI,	TREAIQHESGILG,	EAIQHESGILGPL,	QHESGILGPLLYG,
SGILGPLLYGEVG,	GILGPLLYGEVGD,	GPLLYGEVGDTLL,	PLLYGEVGDTLLI,
LLYGEVGDTLLII,	GEVGDTLLIIFKN,	DTLLIIFKNQASR,	TLLIIFKNQASRP,
LLIIFKNQASRPY,	LIIFKNQASRPYN,	IIFKNQASRPYNI,	SRPYNIYPHGITD,
RPYNIYPHGITDV,	YNIYPHGITDVRP,	NIYPHGITDVRPL,	PHGITDVRPLYSR,
HGITDVRPLYSRR,	TDVRPLYSRRLPK,	RPLYSRRLPKGVK,	PLYSRRLPKGVKH,
RRLPKGVKHLKDF,	KGVKHLKDFPILP,	KHLKDFPILPGEI,	LKDFPILPGEIFK,
KDFPILPGEIFKY,	FPILPGEIFKYKW,	PILPGEIFKYKWT,	GEIFKYKWTVTVE,
EIFKYKWTVTVED,	FKYKWTVTVEDGP,	YKWTVTVEDGPTK,	WTVTVEDGPTKSD,
VTVEDGPTKSDPR,	GPTKSDPRCLTRY,	SDPRCLTRYYSSF,	RCLTRYYSSFVNM,

Figure 1 (continued)

TRYYSSFVNMERD, RYYSSFVNMERDL, SSFVNMERDLASG, SFVNMERDLASGL,
VNMERDLASGLIG, NMERDLASGLIGP, RDLASGLIGPLLI, DLASGLIGPLLIC,
LASGLIGPLLICY, SGLIGPLLICYKE, GLIGPLLICYKES, GPLLICYKESVDQ,
PLLICYKESVDQR, LLICYKESVDQRG, ICYKESVDQRGNQ, CYKESVDQRGNQI,
KESVDQRGNQIMS, ESVDQRGNQIMSD, NQIMSDKRNVILF, QIMSDKRNVILFS,
RNVILFSVFDENR, NVILFSVFDENRS, VILFSVFDENRSW, ILFSVFDENRSWY,
LFSVFDENRSWYL, FSVFDENRSWYLT, SVFDENRSWYLTE, RSWYLTENIQRFL,
SWYLTENIQRFLP, WYLTENIQRFLPN, ENIQRFLPNPAGV, QRFLPNPAGVQLE,
RFLPNPAGVQLED, AGVQLEDPEFQAS, GVQLEDPEFQASN, VQLEDPEFQASNI,
QLEDPEFQASNIM, PEFQASNIMHSIN, SNIMHSINGYVFD, NIMHSINGYVFDS,
HSINGYVFDSLQL, INGYVFDSLQLSV, NGYVFDSLQLSVC, GYVFDSLQLSVCL,
YVFDSLQLSVCLH, VFDSLQLSVCLHE, DSLQLSVCLHEVA, LQLSVCLHEVAYW,
LSVCLHEVAYWYI, VCLHEVAYWYILS, HEVAYWYILSIGA, VAYWYILSIGAQT,
AYWYILSIGAQTD, YWYILSIGAQTDF, WYILSIGAQTDFL, YILSIGAQTDFLS,
ILSIGAQTDFLSV, LSIGAQTDFLSVF, IGAQTDFLSVFFS, TDFLSVFFSGYTF,
DFLSVFFSGYTFK, LSVFFSGYTFKHK, SVFFSGYTFKHKM, VFFSGYTFKHKMV,
FSGYTFKHKMVYE, SGYTFKHKMVYED, YTFKHKMVYEDTL, HKMVYEDTLTLFP,
KMVYEDTLTLFPF, MVYEDTLTLFPFS, DTLTLFPFSGETV, LTLFPFSGETVFM,
TLFPFSGETVFMS, FPFSGETVFMSME, SGETVFMSMENPG, ETVFMSMENPGLW,
TVFMSMENPGLWI, VFMSMENPGLWIL, MSMENPGLWILGC, PGLWILGCHNSDF,
GLWILGCHNSDFR, LWILGCHNSDFRN, WILGCHNSDFRNR, GCHNSDFRNRGMT,
CHNSDFRNRGMTA, SDFRNRGMTALLK, RGMTALLKVSSCD, TALLKVSSCDKNT,
ALLKVSSCDKNTG, LKVSSCDKNTGDY, GDYYEDSYEDISA, DYYEDSYEDISAY,
EDSYEDISAYLLS, DSYEDISAYLLSK, EDISAYLLSKNNA, DISAYLLSKNNAI,
ISAYLLSKNNAIE, SAYLLSKNNAIEP, AYLLSKNNAIEPR, YLLSKNNAIEPRS,
SKNNAIEPRSFSQ, NAIEPRSFSQNSR, RSFSQNSRHPSTR, KQFNATTIPENDI,
TTIPENDIEKTDP, NDIEKTDPWFAHR, TDPWFAHRTPMPK, DPWFAHRTPMPKI,
PWFAHRTPMPKIQ, TPMPKIQNVSSSD, PKIQNVSSSDLLM, QNVSSSDLLMLLR,
NVSSSDLLMLLRQ, SDLLMLLRQSPTP, DLLMLLRQSPTPH, LLMLLRQSPTPHG,
LMLLRQSPTPHGL, MLLRQSPTPHGLS, HGLSLSDLQEAKY, GLSLSDLQEAKYE,
LSLSDLQEAKYET, SDLQEAKYETFSD, AKYETFSDDPSPG, ETFSDDPSPGAID,
PSPGAIDSNNSLS, SPGAIDSNNSLSE, GAIDSNNSLSEMT, NSLSEMTHFRPQL,
SEMTHFRPQLHHS, THFRPQLHHSGDM, PQLHHSGDMVFTP, HSGDMVFTPESGL,
GDMVFTPESGLQL, DMVFTPESGLQLR, MVFTPESGLQLRL, SGLQLRLNEKLGT,
LQLRLNEKLGTTA, LRLNEKLGTTAAT, RLNEKLGTTAATE, EKLGTTAATELKK,
KLGTTAATELKKL, TAATELKKLDFKV, TELKKLDFKVSST, ELKKLDFKVSSTS,
KKLDFKVSSTSNN, KLDFKVSSTSNNL, LDFKVSSTSNNLI, FKVSSTSNNLIST,
TSNNLISTIPSDN, NNLISTIPSDNLA, NLISTIPSDNLAA, STIPSDNLAAGTD,
SDNLAAGTDNTSS, DNLAAGTDNTSSL, LAAGTDNTSSLGP, DNTSSLGPPSMPV,
SSLGPPSMPVHYD, PSMPVHYDSQLDT, MPVHYDSQLDTTL, PVHYDSQLDTTLF,
VHYDSQLDTTLFG, HYDSQLDTTLFGK, SQLDTTLFGKKSS, TTLFGKKSSPLTE,
TLFGKKSSPLTES, SPLTESGGPLSLS, GPLSLSEENNDSK, LSLSEENNDSKLL,
SEENNDSKLLESG, NDSKLLESGLMNS, SKLLESGLMNSQE, KLLESGLMNSQES,
SGLMNSQESSWGK, GLMNSQESSWGKN, LMNSQESSWGKNV, SSWGKNVSSTESG,
SWGKNVSSTESGR, KNVSSTESGRLFK, GRLFKGKRAHGPA, RLFKGKRAHGPAL,
FKGKRAHGPALLT, AHGPALLTKDNAL, HGPALLTKDNALF, PALLTKDNALFKV,
ALLTKDNALFKVS, DNALFKVSISLLK, NALFKVSISLLKT, ALFKVSISLLKTN,
FKVSISLLKTNKT, KVSISLLKTNKTS, VSISLLKTNKTSN, SISLLKTNKTSNN,
ISLLKTNKTSNNS, SLLKTNKTSNNSA, LLKTNKTSNNSAT, KTSNNSATNRKTH,
NRKTHIDGPSLLI, THIDGPSLLIENS, DGPSLLIENSPSV, GPSLLIENSPSVW,
PSLLIENSPSVWQ, SLLIENSPSVWQN, LLIENSPSVWQNI, IENSPSVWQNILE,
PSVWQNILESDTE, SVWQNILESDTEF, QNILESDTEFKKV, NILESDTEFKKVT,
DTEFKKVTPLIHD, TEFKKVTPLIHDR, FKKVTPLIHDRML, KKVTPLIHDRMLM,
VTPLIHDRMLMDK, TPLIHDRMLMDKN, PLIHDRMLMDKNA, IHDRMLMDKNATA,
HDRMLMDKNATAL, DRMLMDKNATALR, RMLMDKNATALRL, MLMDKNATALRLN,
DKNATALRLNHMS, NATALRLNHMSNK, TALRLNHMSNKTT, LRLNHMSNKTTSS,
NHMSNKTTSSKNM, KNATALRLNHMSN, ALRLNHMSNKTTS, SKNMEMVQQKKEG,
KNMEMVQQKKEGP, MEMVQQKKEGPIP, EMVQQKKEGPIPP, EGPIPPDAQNPDM,
GPIPPDAQNPDMS, PDAQNPDMSFFKM, NPDMSFFKMLFLP, PDMSFFKMLFLPE,
MSFFKMLFLPESA, SFFKMLFLPESAR, FFKMLFLPESARW, FKMLFLPESARWI,
KMLFLPESARWIQ, MLFLPESARWIQR, LFLPESARWIQRT, SARWIQRTHGKNS,
ARWIQRTHGKNSL, RWIQRTHGKNSLN, IQRTHGKNSLNSG, NSLNSGQGPSPKQ,
PKQLVSLGPEKSV, KQLVSLGPEKSVE, QLVSLGPEKSVEG, LVSLGPEKSVEGQ,
VSLGPEKSVEGQN, LGPEKSVEGQNFL, GPEKSVEGQNFLS, KSVEGQNFLSEKN,

Figure 1 (continued)

SVEGQNFLSEKNK,	GQNFLSEKNKVVV,	QNFLSEKNKVVVG,	NFLSEKNKVVVGK,
NKVVVGKGEFTKD,	KVVVGKGEFTKDV,	VVVGKGEFTKDVG,	KGEFTKDVGLKEM,
GEFTKDVGLKEMV,	KDVGLKEMVFPSS,	VGLKEMVFPSSRN,	GLKEMVFPSSRNL,
LKEMVFPSSRNLF,	KEMVFPSSRNLFL,	EMVFPSSRNLFLT,	MVFPSSRNLFLTN,
SSRNLFLTNLDNL,	SRNLFLTNLDNLH,	RNLFLTNLDNLHE,	NLFLTNLDNLHEN,
LFLTNLDNLHENN,	LTNLDNLHENNTH,	TNLDNLHENNTHN,	NLDNLHENNTHNQ,
LDNLHENNTHNQE,	DNLHENNTHNQEK,	EKKIQEEIEKKET,	KKIQEEIEKKETL,
QEEIEKKETLIQE,	EEIEKKETLIQEN,	IEKKETLIQENVV,	KKETLIQENVVLP,
ETLIQENVVLPQI,	TLIQENVVLPQIH,	IQENVVLPQIHTV,	ENVVLPQIHTVTG,
NVVLPQIHTVTGT,	VVLPQIHTVTGTK,	LPQIHTVTGTKNF,	PQIHTVTGTKNFM,
IHTVTGTKNFMKN,	HTVTGTKNFMKNL,	KNFMKNLFLLSTR,	NFMKNLFLLSTRQ,
FMKNLFLLSTRQN,	MKNLFLLSTRQNV,	KNLFLLSTRQNVE,	NLFLLSTRQNVEG,
LFLLSTRQNVEGS,	FLLSTRQNVEGSY,	RQNVEGSYDGAYA,	QNVEGSYDGAYAP,
EGSYDGAYAPVLQ,	GSYDGAYAPVLQD,	DGAYAPVLQDFRS,	GAYAPVLQDFRSL,
YAPVLQDFRSLND,	APVLQDFRSLNDS,	PVLQDFRSLNDST,	LQDFRSLNDSTNR,
QDFRSLNDSTNRT,	DFRSLNDSTNRTK,	FRSLNDSTNRTKK,	RSLNDSTNRTKKH,
AHFSKKGEEENLE,	EENLEGLGNQTKQ,	ENLEGLGNQTKQI,	LEGLGNQTKQIVE,
EGLGNQTKQIVEK,	LGNQTKQIVEKYA,	KQIVEKYACTTRI,	QIVEKYACTTRIS,
EKYACTTRISPNT,	TTRISPNTSQQNF,	TRISPNTSQQNFV,	NTSQQNFVTQRSK,
TSQQNFVTQRSKR,	QQNFVTQRSKRAL,	QNFVTQRSKRALK,	NFVTQRSKRALKQ,
QRSKRALKQFRLP,	RALKQFRLPLEET,	KQFRLPLEETELE,	QFRLPLEETELEK,
FRLPLEETELEKR,	LPLEETELEKRII,	PLEETELEKRIIV,	LEETELEKRIIVD,
TELEKRIIVDDTS,	EKRIIVDDTSTQW,	KRIIVDDTSTQWS,	RIIVDDTSTQWSK,
IIVDDTSTQWSKN,	VDDTSTQWSKNMK,	TQWSKNMKHLTPS,	SKNMKHLTPSTLT,
KNMKHLTPSTLTQ,	KHLTPSTLTQIDY,	PSTLTQIDYNEKE,	STLTQIDYNEKEK,
LTQIDYNEKEKGA,	TQIDYNEKEKGAI,	QIDYNEKEKGAIT,	IDYNEKEKGAITQ,
EKEKGAITQSPLS,	GAITQSPLSDCLT,	SPLSDCLTRSHSI,	SDCLTRSHSIPQA,
DCLTRSHSIPQAN,	SHSIPQANRSPLP,	HSIPQANRSPLPI,	RSPLPIAKVSSFP,
SPLPIAKVSSFPS,	PLPIAKVSSFPSI,	LPIAKVSSFPSIR,	IAKVSSFPSIRPI,
AKVSSFPSIRPIY,	VSSFPSIRPIYLT,	SSFPSIRPIYLTR,	FPSIRPIYLTRVL,
PSIRPIYLTRVLF,	SIRPIYLTRVLFQ,	RPIYLTRVLFQDN,	PIYLTRVLFQDNS,
IYLTRVLFQDNSS,	LTRVLFQDNSSHL,	TRVLFQDNSSHLP,	RVLFQDNSSHLPA,
VLFQDNSSHLPAA,	QDNSSHLPAASYR,	NSSHLPAASYRKK,	SSHLPAASYRKKD,
SHLPAASYRKKDS,	AASYRKKDSGVQE,	ASYRKKDSGVQES,	KKDSGVQESSHFL,
KDSGVQESSHFLQ,	DSGVQESSHFLQG,	SGVQESSHFLQGA,	VQESSHFLQGAKK,
SHFLQGAKKNNLS,	HFLQGAKKNNLSL,	NNLSLAILTLEMT,	NLSLAILTLEMTG,
LSLAILTLEMTGD,	LAILTLEMTGDQR,	AILTLEMTGDQRE,	LTLEMTGDQREVG,
TLEMTGDQREVGS,	LEMTGDQREVGSL,	TGDQREVGSLGTS,	QREVGSLGTSATN,
REVGSLGTSATNS,	VGSLGTSATNSVT,	GSLGTSATNSVTY,	KNNLSLAILTLEM,
NSVTYKKVENTVL,	SVTYKKVENTVLP,	VTYKKVENTVLPK,	KKVENTVLPKPDL,
NTVLPKPDLPKTS,	PDLPKTSGKVELL,	SGKVELLPKVHIY,	GKVELLPKVHIYQ,
VELLPKVHIYQKD,	ELLPKVHIYQKDL,	LPKVHIYQKDLFP,	PKVHIYQKDLFPT,
VHIYQKDLFPTET,	HIYQKDLFPTETS,	KDLFPTETSNGSP,	DLFPTETSNGSPG,
PGHLDLVEGSLLQ,	GHLDLVEGSLLQG,	LDLVEGSLLQGTE,	DLVEGSLLQGTEG,
VEGSLLQGTEGAI,	EGSLLQGTEGAIK,	GSLLQGTEGAIKW,	SLLQGTEGAIKWN,
GAIKWNEANRPGK,	AIKWNEANRPGKV,	IKWNEANRPGKVP,	RPGKVPFLRVATE,
GKVPFLRVATESS,	KVPFLRVATESSA,	VPFLRVATESSAK,	PFLRVATESSAKT,
FLRVATESSAKTP,	LRVATESSAKTPS,	VATESSAKTPSKL,	SKLLDPLAWDNHY,
KLLDPLAWDNHYG,	LLDPLAWDNHYGT,	LDPLAWDNHYGTQ,	DPLAWDNHYGTQI,
PLAWDNHYGTQIP,	LAWDNHYGTQIPK,	DNHYGTQIPKEEW,	NHYGTQIPKEEWK,
GTQIPKEEWKSQE,	TQIPKEEWKSQEK,	KEEWKSQEKSPEK,	EEWKSQEKSPEKT,
KSQEKSPEKTAFK,	SQEKSPEKTAFKK,	KTAFKKKDTILSL,	QEKSPEKTAFKKK,
KSPEKTAFKKKDT,	SPEKTAFKKKDTI,	KTAFKKKDTILSL,	TAFKKKDTILSLN,
AFKKKDTILSLNA,	DTILSLNACESNH,	TILSLNACESNHA,	ILSLNACESNHAI,
LSLNACESNHAIA,	HAIAAINEGQNKP,	AIAAINEGQNKPE,	IAAINEGQNKPEI,
AAINEGQNKPEIE,	GQNKPEIEVTWAK,	QNKPEIEVTWAKQ,	GQNKPEIEVTWAK,
QNKPEIEVTWAKQ,	PEIEVTWAKQGRT,	EIEVTWAKQGRTE,	IEVTWAKQGRTER,
EVTWAKQGRTERL,	VTWAKQGRTERLC,	TERLCSQNPPVLK,	ERLCSQNPPVLKR,
NPPVLKRHQREIT,	PPVLKRHQREITR,	PVLKRHQREITRT,	LKRHQREITRTTL,
KRHQREITRTTLQ,	REITRTTLQSDQE,	TTLQSDQEEIDYD,	QEEIDYDDTISVE,
EEIDYDDTISVEM,	EIDYDDTISVEMK,	IDYDDTISVEMKK,	DTISVEMKKEDFD,
TISVEMKKEDFDI,	ISVEMKKEDFDIY,	SVEMKKEDFDIYD,	VEMKKEDFDIYDE,
EDFDIYDEDENQS,	DFDIYDEDENQSP,	FDIYDEDENQSPR,	DIYDEDENQSPRS,

Figure 1 (continued)

YDEDENQSPRSFQ, PRSFQKKTRHYFI, RSFQKKTRHYFIA, TRHYFIAAVERLW,
RHYFIAAVERLWD, HYFIAAVERLWDY, YFIAAVERLWDYG, IAAVERLWDYGMS,
AAVERLWDYGMSS, ERLWDYGMSSSPH, RLWDYGMSSSPHV, LWDYGMSSSPHVL,
WDYGMSSSPHVLR, YGMSSSPHVLRNR, MSSSPHVLRNRAQ, SSSPHVLRNRAQS,
PHVLRNRAQSGSV, HVLRNRAQSGSVP, RAQSGSVPQFKKV, QSGSVPQFKKVVF,
GSVPQFKKVVFQE, VPQFKKVVFQEFT, PQFKKVVFQEFTD, FKKVVFQEFTDGS,
KKVVFQEFTDGSF, KVVFQEFTDGSFT, VVFQEFTDGSFTQ, VFQEFTDGSFTQP,
QEFTDGSFTQPLY, GSFTQPLYRGELN, QPLYRGELNEHLG, PLYRGELNEHLGL,
GELNEHLGLLGPY, LNEHLGLLGPYIR, NEHLGLLGPYIRA, EHLGLLGPYIRAE,
LGLLGPYIRAEVE, GLLGPYIRAEVED, LGPYIRAEVEDNI, GPYIRAEVEDNIM,
PYIRAEVEDNIMV, YIRAEVEDNIMVT, RAEVEDNIMVTFR, AEVEDNIMVTFRN,
EDNIMVTFRNQAS, DNIMVTFRNQASR, NIMVTFRNQASRP, IMVTFRNQASRPY,
MVTFRNQASRPYS, VTFRNQASRPYSF, ASRPYSFYSSLIS, SRPYSFYSSLISY,
RPYSFYSSLISYE, YSFYSSLISYEED, SFYSSLISYEEDQ, YSSLISYEEDQRQ,
SSLISYEEDQRQG, SLISYEEDQRQGA, LISYEEDQRQGAE, ISYEEDQRQGAEP,
KNFVKPNETKTYF, NFVKPNETKTYFW, KTYFWKVQHHMAP, TYFWKVQHHMAPT,
YFWKVQHHMAPTK, WKVQHHMAPTKDE, HHMAPTKDEFDCK, TKDEFDCKAWAYF,
DEFDCKAWAYFSD, KAWAYFSDVDLEK, WAYFSDVDLEKDV, AYFSDVDLEKDVH,
SDVDLEKDVHSGL, DVDLEKDVHSGLI, VDLEKDVHSGLIG, LEKDVHSGLIGPL,
KDVHSGLIGPLLV, DVHSGLIGPLLVC, VHSGLIGPLLVCH, SGLIGPLLVCHTN,
GLIGPLLVCHTNT, IGPLLVCHTNTLN, GPLLVCHTNTLNP, PLLVCHTNTLNPA,
LLVCHTNTLNPAH, NTLNPAHGRQVTV, AHGRQVTVQEFAL, RQVTVQEFALFFT,
VTVQEFALFFTIF, TVQEFALFFTIFD, QEFALFFTIFDET, FALFFTIFDETKS,
ALFFTIFDETKSW, LFFTIFDETKSWY, FTIFDETKSWYFT, TIFDETKSWYFTE,
KSWYFTENMERNC, SWYFTENMERNCR, WYFTENMERNCRA, FTENMERNCRAPC,
ENMERNCRAPCNI, PCNIQMEDPTFKE, CNIQMEDPTFKEN, IQMEDPTFKENYR,
PTFKENYRFHAIN, ENYRFHAINGYIM, NYRFHAINGYIMD, YRFHAINGYIMDT,
HAINGYIMDTLPG, AINGYIMDTLPGL, NGYIMDTLPGLVM, GYIMDTLPGLVMA,
YIMDTLPGLVMAQ, DTLPGLVMAQDQR, TLPGLVMAQDQRI, PGLVMAQDQRIRW,
GLVMAQDQRIRWY, LVMAQDQRIRWYL, MAQDQRIRWYLLS, QRIRWYLLSMGSN,
IRWYLLSMGSNEN, RWYLLSMGSNENI, WYLLSMGSNENIH, YLLSMGSNENIHS,
LSMGSNENIHSIH, GSNENIHSIHFSG, ENIHSIHFSGHVF, HSIHFSGHVFTVR,
IHFSGHVFTVRKK, HFSGHVFTVRKKE, GHVFTVRKKEEYK, HVFTVRKKEEYKM,
FTVRKKEEYKMAL, VRKKEEYKMALYN, KEEYKMALYNLYP, EEYKMALYNLYPG,
YKMALYNLYPGVF, MALYNLYPGVFET, ALYNLYPGVFETV, YNLYPGVFETVEM,
NLYPGVFETVEML, PGVFETVEMLPSK, GVFETVEMLPSKA, FETVEMLPSKAGI,
ETVEMLPSKAGIW, VEMLPSKAGIWRV, EMLPSKAGIWRVE, MLPSKAGIWRVEC,
AGIWRVECLIGEH, GIWRVECLIGEHL, WRVECLIGEHLHA, ECLIGEHLHAGMS,
CLIGEHLHAGMST, EHLHAGMSTLFLV, HLHAGMSTLFLVY, AGMSTLFLVYSNK,
STLFLVYSNKCQT, TLFLVYSNKCQTP, LFLVYSNKCQTPL, FLVYSNKCQTPLG,
LVYSNKCQTPLGM, YSNKCQTPLGMAS, QTPLGMASGHIRD, TPLGMASGHIRDF,
LGMASGHIRDFQI, SGHIRDFQITASG, GHIRDFQITASGQ, IRDFQITASGQYG,
RDFQITASGQYGQ, FQITASGQYGQWA, EHLHAGMSTLFLV, HLHAGMSTLFLVY,
AGMSTLFLVYSNK, STLFLVYSNKCQT, TLFLVYSNKCQTP, LFLVYSNKCQTPL,
FLVYSNKCQTPLG, LVYSNKCQTPLGM, YSNKCQTPLGMAS, QTPLGMASGHIRD,
TPLGMASGHIRDF, LGMASGHIRDFQI, SGHIRDFQITASG, GHIRDFQITASGQ,
IRDFQITASGQYG, RDFQITASGQYGQ, FQITASGQYGQWA, TASGQYGQWAPKL,
SGQYGQWAPKLAR, GQYGQWAPKLARL, GQWAPKLARLHYS, QWAPKLARLHYSG,
PKLARLHYSGSIN, ARLHYSGSINAWS, LHYSGSINAWSTK, GSINAWSTKEPFS,
NAWSTKEPFSWIK, EPFSWIKVDLLAP, FSWIKVDLLAPMI, SWIKVDLLAPMII,
WIKVDLLAPMIIH, IKVDLLAPMIIHG, VDLLAPMIIHGIK, DLLAPMIIHGIKT,
LLAPMIIHGIKTQ, APMIIHGIKTQGA, PMIIHGIKTQGAR, MIIHGIKTQGARQ,
HGIKTQGARQKFS, GIKTQGARQKFSS, IKTQGARQKFSSL, GARQKFSSLYISQ,
QKFSSLYISQFII, FSSLYISQFIIMY, SSLYISQFIIMYS, SLYISQFIIMYSL,
LYISQFIIMYSLD, YISQFIIMYSLDG, SQFIIMYSLDGKK, QFIIMYSLDGKKW,
FIIMYSLDGKKWQ, IIMYSLDGKKWQT, IMYSLDGKKWQTY, YSLDGKKWQTYRG,
KKWQTYRGNSTGT, QTYRGNSTGTLMV, GTLMVFFGNVDSS, TLMVFFGNVDSSG,
LMVFFGNVDSSGI, MVFFGNVDSSGIK, VFFGNVDSSGIKH, FFGNVDSSGIKHN,
GNVDSSGIKHNIF, VDSSGIKHNIFNP, SGIKHNIFNPPII, GIKHNIFNPPIIA,
IKHNIFNPPIIAR, KHNIFNPPIIARY, HNIFNPPIIARYI, NIFNPPIIARYIR,
NPPIIARYIRLHP, PPIIARYIRLHPT, PIIARYIRLHPTH, ARYIRLHPTHYSI,
RYIRLHPTHYSIR, IRLHPTHYSIRST, THYSIRSTLRMEL, YSIRSTLRMELMG,
STLRMELMGCDLN, TLRMELMGCDLNS, LRMELMGCDLNSC, MELMGCDLNSCSM,
ELMGCDLNSCSMP, LMGCDLNSCSMPL, CDLNSCSMPLGME, CSMPLGMESKAIS,

Figure 1 (continued)

SMPLGMESKAISD,	MPLGMESKAISDA,	LGMESKAISDAQI,	GMESKAISDAQIT,
SKAISDAQITASS,	KAISDAQITASSY,	AISDAQITASSYF,	DAQITASSYFTNM,
AQITASSYFTNMF,	TASSYFTNMFATW,	SSYFTNMFATWSP,	SYFTNMFATWSPS,
TNMFATWSPSKAR,	NMFATWSPSKARL,	FATWSPSKARLHL,	ATWSPSKARLHLQ,
PSKARLHLQGRSN,	ARLHLQGRSNAWR,	LHLQGRSNAWRPQ,	QGRSNAWRPQVNN,
NAWRPQVNNPKEW,	PQVNNPKEWLQVD,	NNPKEWLQVDFQK,	KEWLQVDFQKTMK,
EWLQVDFQKTMKV,	LQVDFQKTMKVTG,	VDFQKTMKVTGVT,	KTMKVTGVTTQGV,
MKVTGVTTQGVKS,	TGVTTQGVKSLLT,	VTTQGVKSLLTSM,	QGVKSLLTSMYVK,
GVKSLLTSMYVKE,	KSLLTSMYVKEFL,	SLLTSMYVKEFLI,	LTSMYVKEFLISS,
TSMYVKEFLISSS,	SMYVKEFLISSSQ,	MYVKEFLISSSQD,	YVKEFLISSSQDG,
KEFLISSSQDGHQ,	EFLISSSQDGHQW,	FLISSSQDGHQWT,	ISSSQDGHQWTLF,
SQDGHQWTLFFQN,	GHQWTLFFQNGKV,	HQWTLFFQNGKVK,	WTLFFQNGKVKVF,
TLFFQNGKVKVFQ,	LFFQNGKVKVFQG,	NGKVKVFQGNQDS,	GKVKVFQGNQDSF,
VKVFQGNQDSFTP,	KVFQGNQDSFTPV,	DSFTPVVNSLDPP,	TPVVNSLDPPLLT,
PVVNSLDPPLLTR,	NSLDPPLLTRYLR,	SLDPPLLTRYLRI,	PPLLTRYLRIHPQ,
PLLTRYLRIHPQS,	TRYLRIHPQSWVH,	RYLRIHPQSWVHQ,	LRIHPQSWVHQIA,
HPQSWVHQIALRM,	QSWVHQIALRMEV,	SWVHQIALRMEVL,	WVHQIALRMEVLG,
HQIALRMEVLGCE,	IALRMEVLGCEAQ,	LRMEVLGCEAQDL,	

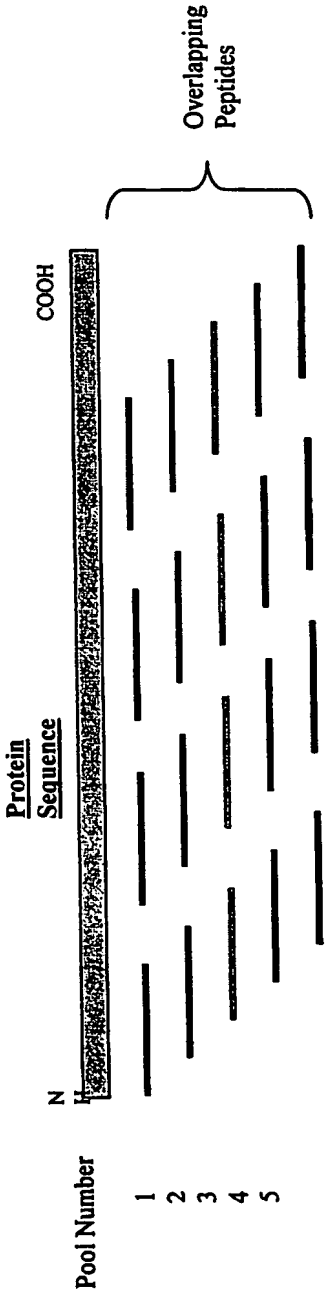

Overlapping Peptides
COOH
Protein Sequence
N
Pool Number
1
2
3
4
5

FIGURE 2

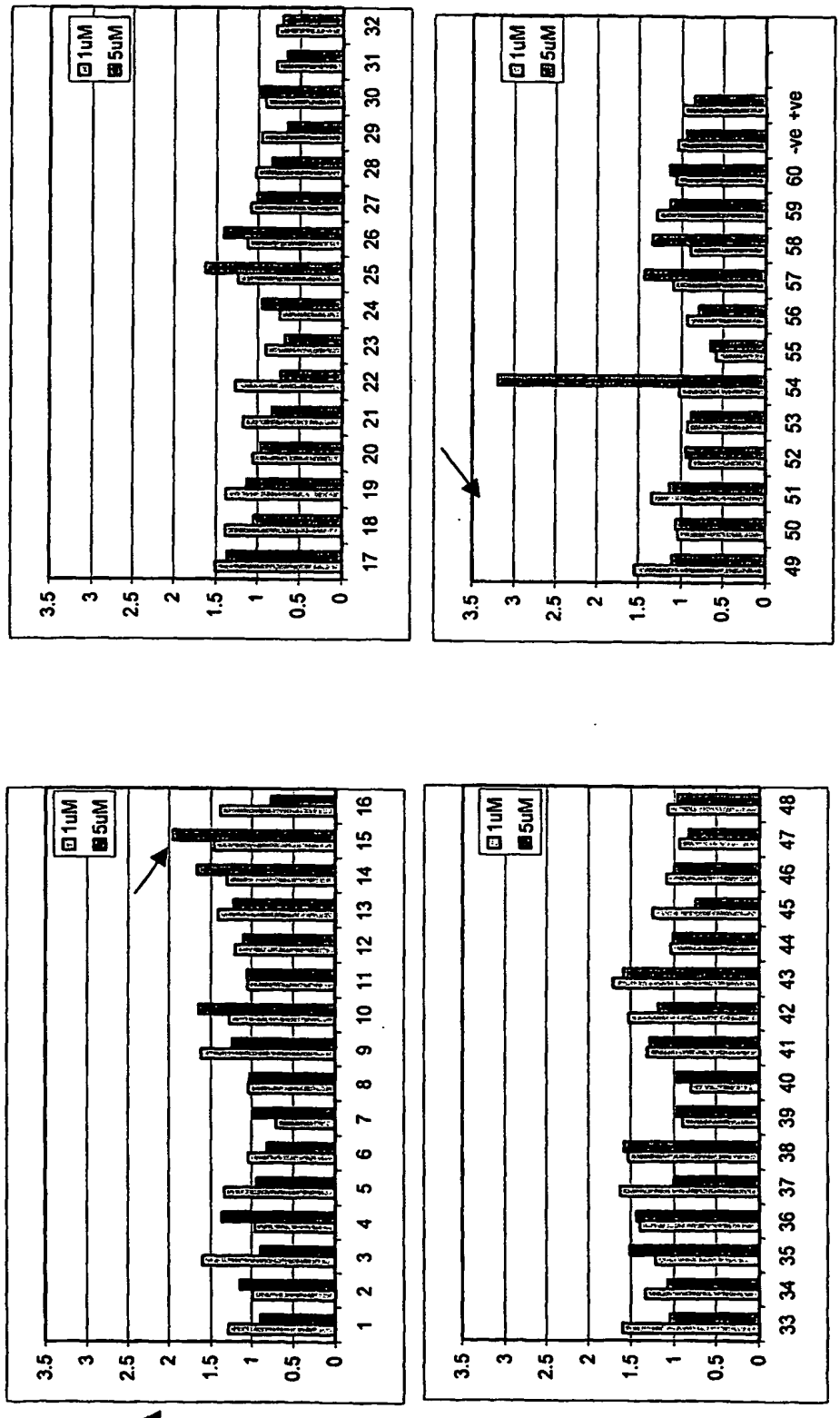
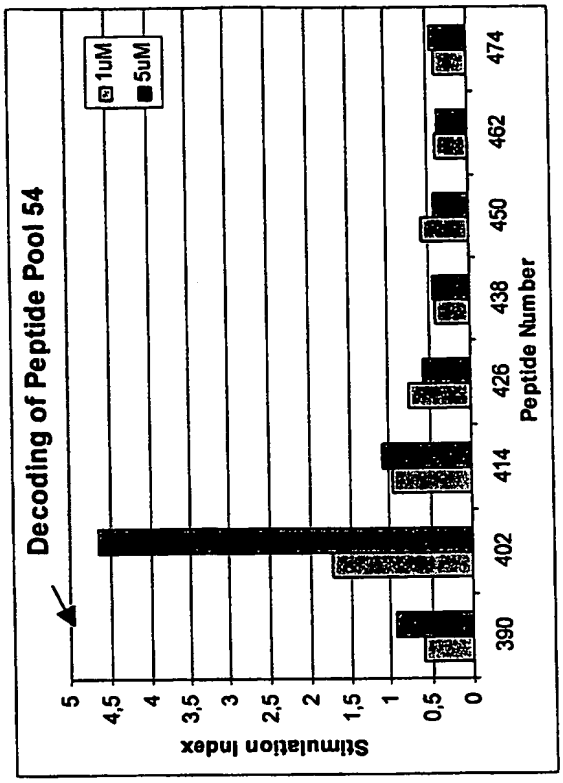


FIGURE 3


Decoding of Peptide Pool 54
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5uM
Stimulation Index
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0,5
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1,5
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3
3,5
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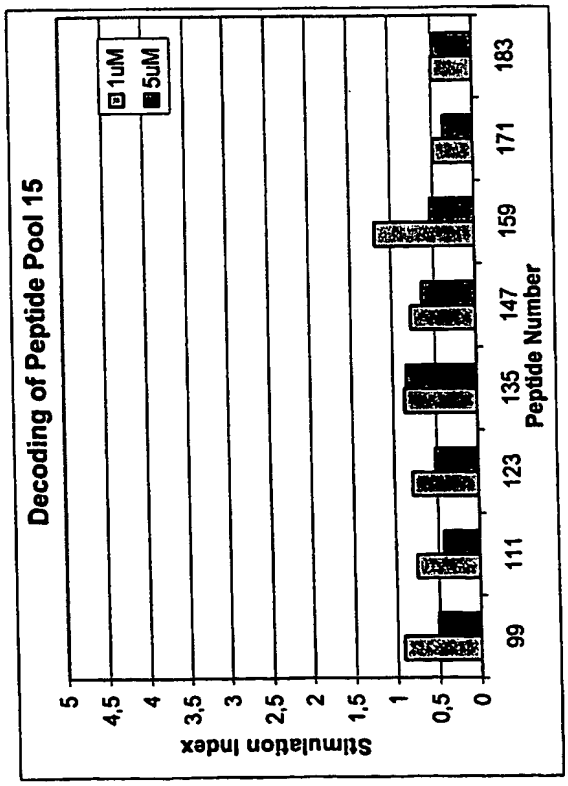
390
402
414
426
438
450
462
474
Peptide Number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1uM
5uM
Stimulation Index
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5
99
111
123
135
147
159
171
183
Peptide Number

FIGURE 4

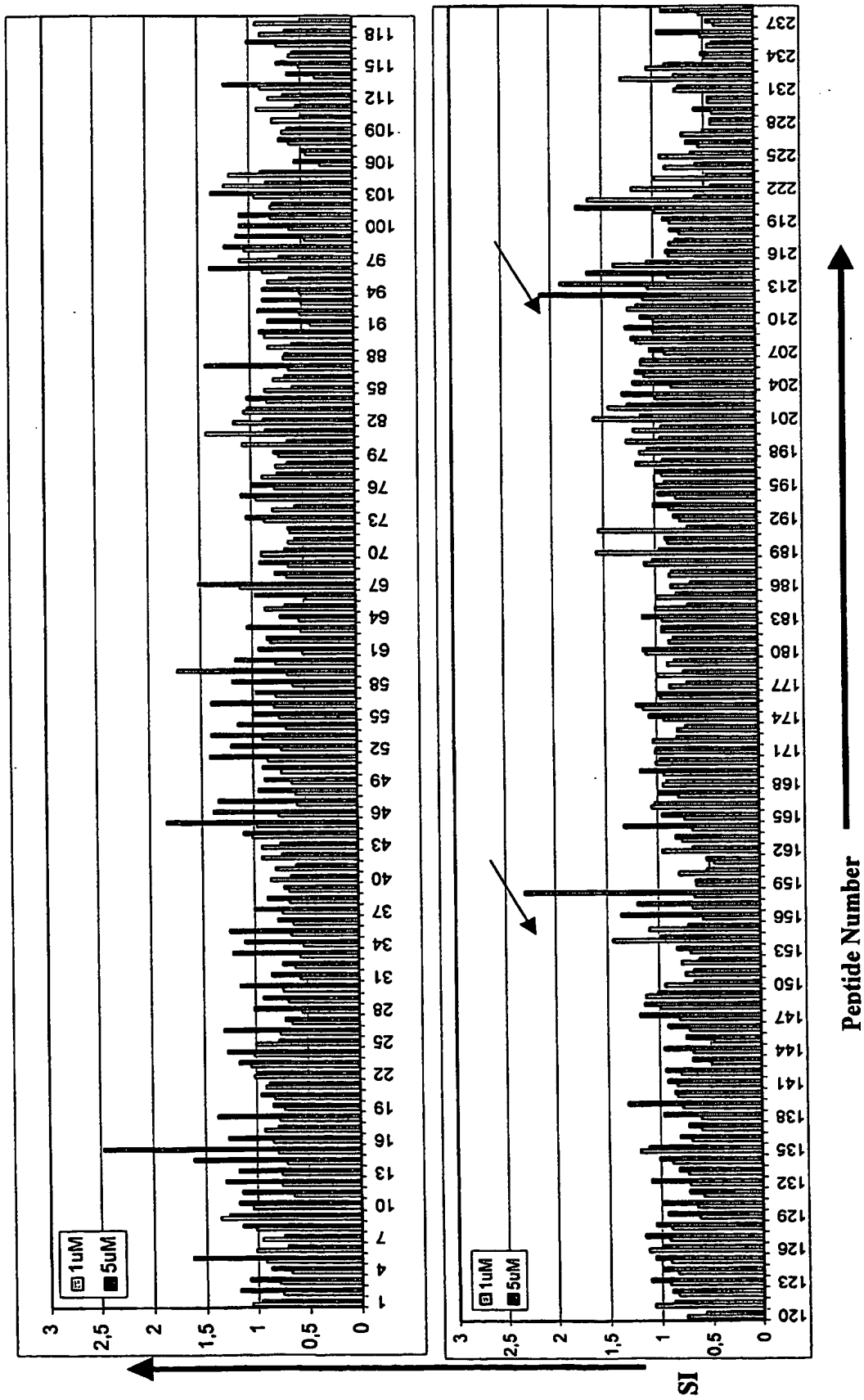


FIGURE 5A

10/511559
PCT/EP03/04063
Rec'd PCT/PTO 15 OCT 2004

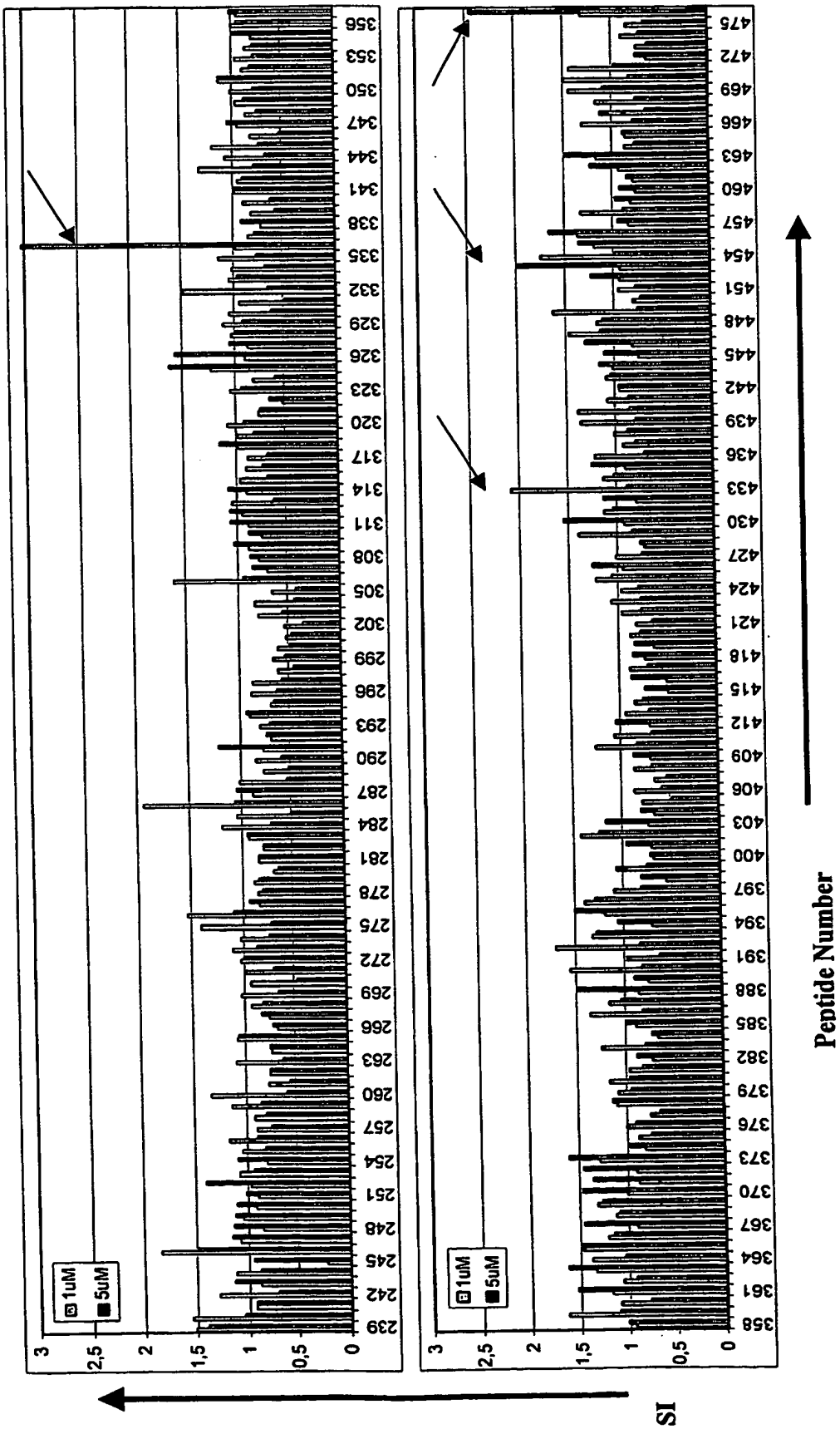


FIGURE 5B

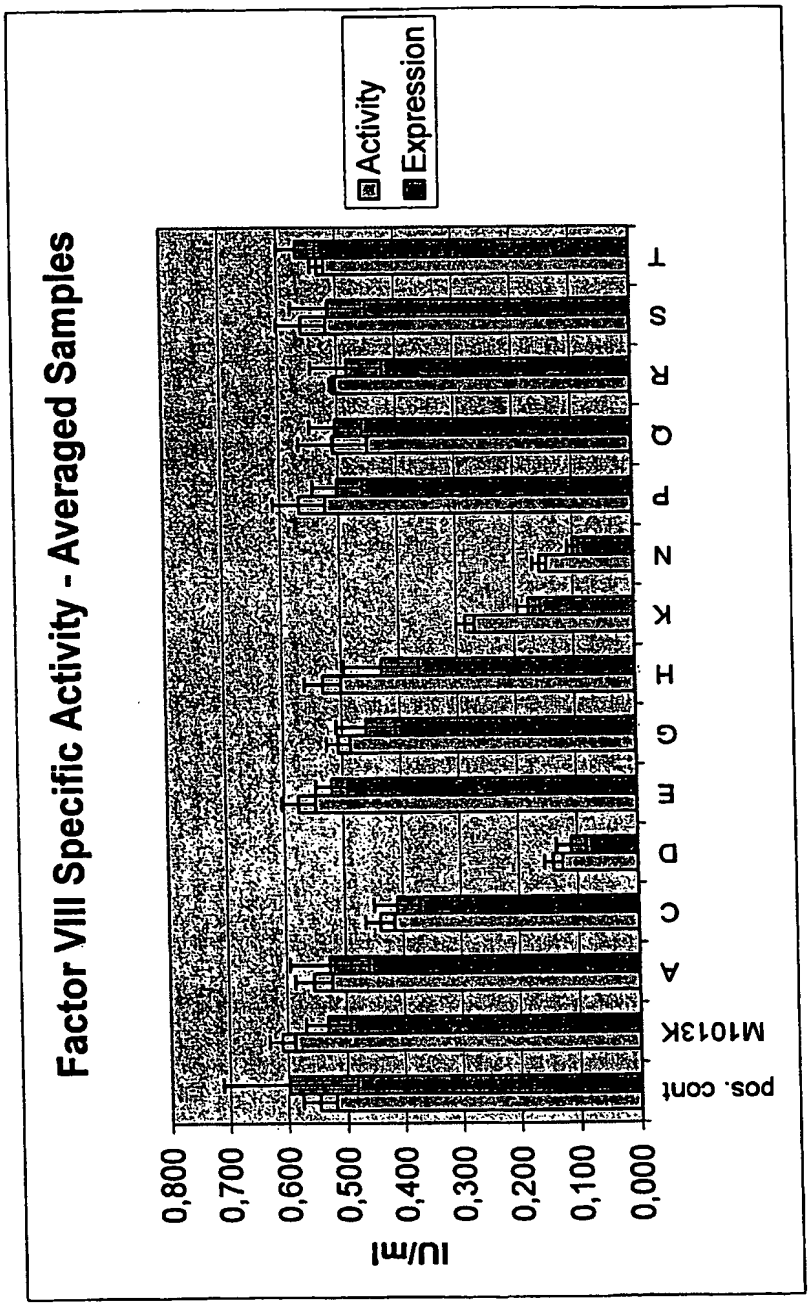

Factor VIII Specific Activity - Averaged Samples
Activity
Expression
IU/ml
0,800
0,700
0,600
0,500
0,400
0,300
0,200
0,100
0,000
pos. cont
M101 3K
A
C
D
E
G
H
K
N
P
Q
R
S
T

FIGURE 6

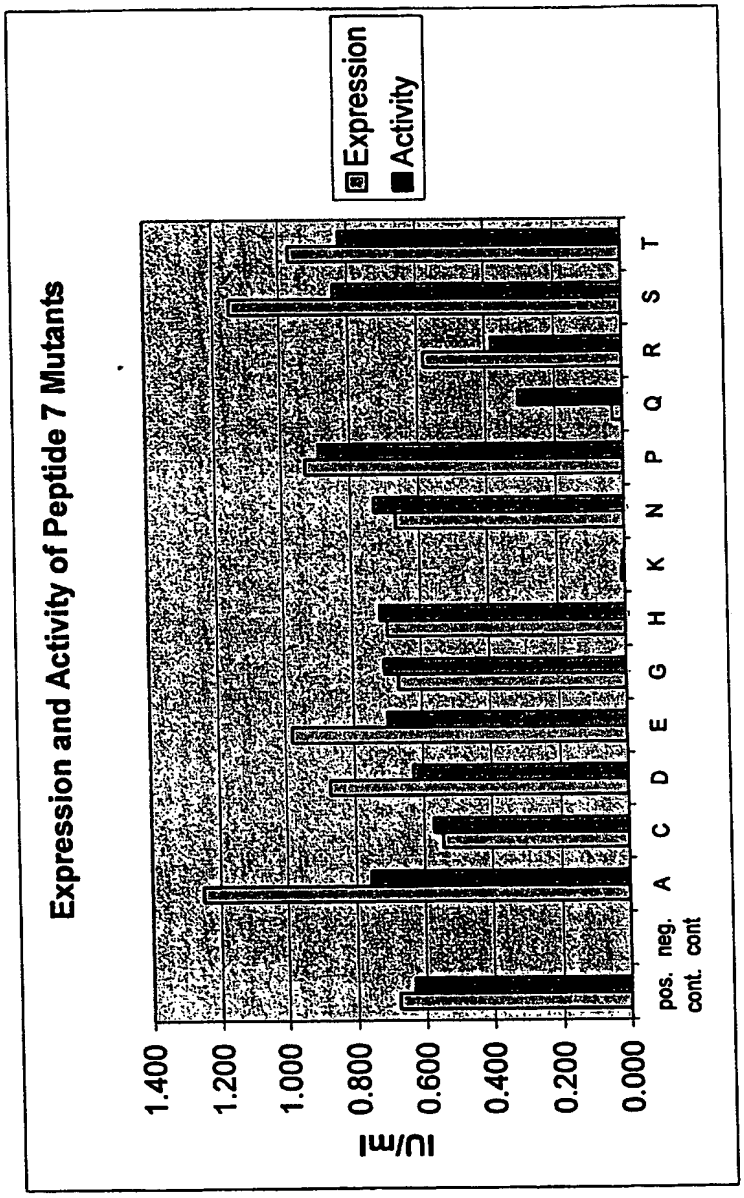
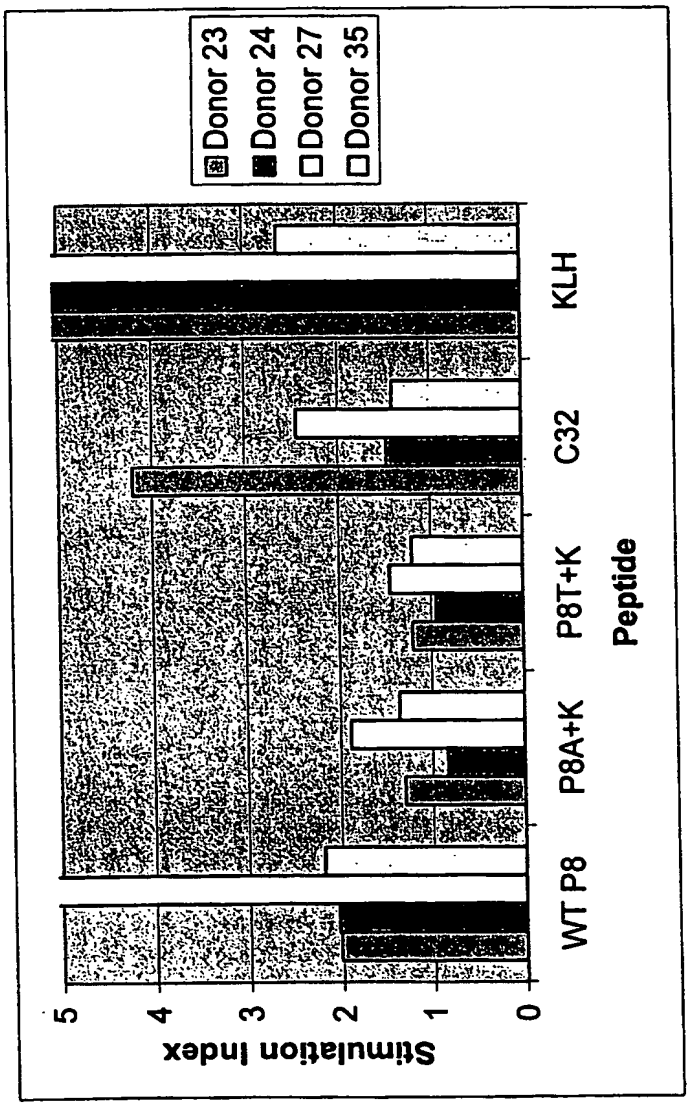


FIGURE 7



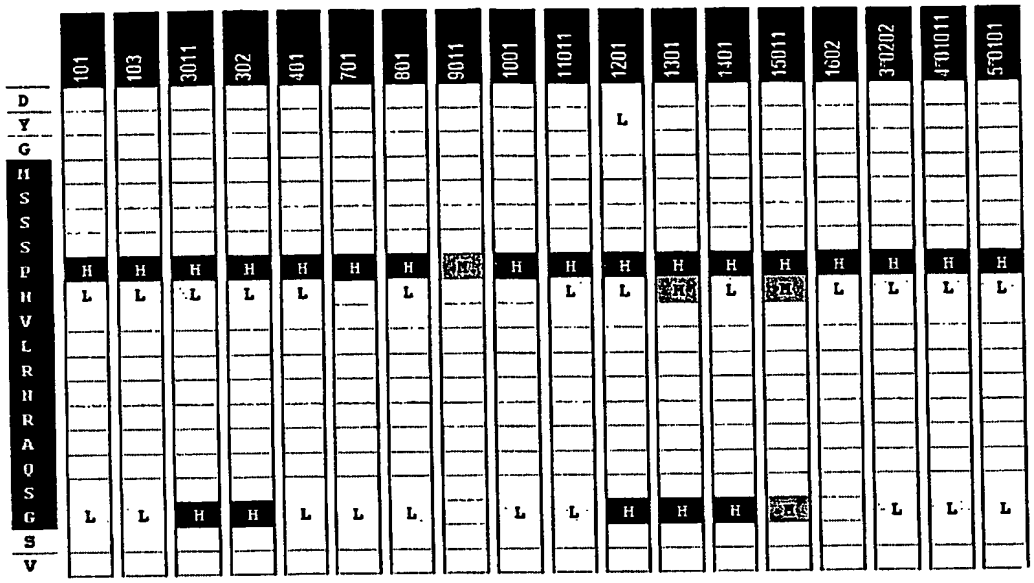
Donor #	MHC Allotype
23	DRB1*04, DRB1*13, DRB3, DRB4*01
24	DRB1*03, DRB1*04, DRB3, DRB4*01
27	DRB1*03, DRB1*15, DRB3, DRB5
35	DRB1*04, DRB1*08, DRB4*01

Peptide	Sequence	Origin
WTP8	CNIQMEDPTFKENYR	FVIII immunogenic peptide P8; residues 1009-1023
P8K+A	CNAQKEDPTFKENYR	Peptide P8 with substitutions $I_{1011}A + M_{1013}K$
P8K+T	CNTQKEDPTFKENYR	Peptide P8 with substitutions $I_{1011}T + M_{1013}K$
C32	PKYVKQNTLKLAT	Control peptide; influenza haemaglutanin residues 307-319
KLH	Whole protein	Control protein; keyhole limpet haemocyanin

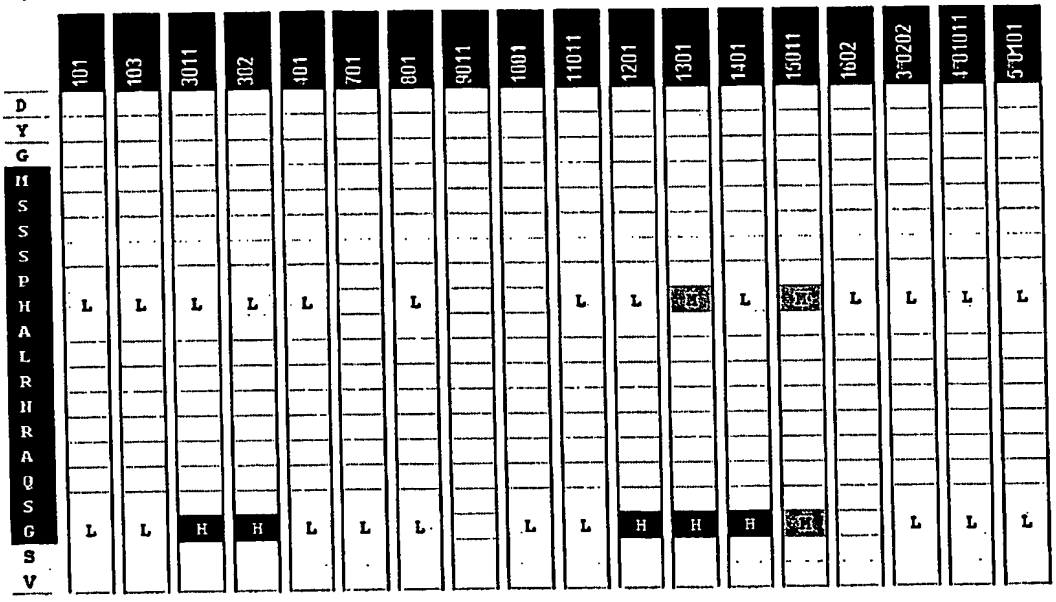
FIGURE 8

FIGURE 9

A) Factor VIII WT (Peptide 7)



B) Factor VIII $V_{823}A$



H High affinity MHC ligand; score > 1,000,000

Medium affinitiy MHC ligand; score 750,001 - 1,000,000

L Low affinity MHC ligand; score 500,000 - 750,000

FIGURE 10


```
1                          25                          50                          75
ATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFNTSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPT
                          100                         125                         150
IQAEVYDTVVITLKNMASHPVSLHAVGVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASD
                          175                         200                         225
PLCLTYSYLSHVDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRDAASA
                          250                         275                         300
RAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNHRQASLEISPITFLTAQTLL
                          325                         350                         375
MDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNEEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVA
                          400                         425                         450
KKHPKTWVHYIAAEEEDWDYAPLVLAPDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILG
                          475                         500                         525
PLLYGEVGDTLLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGPTKSD
                          550                         575                         600
PRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDENRSWYLTENIQRFLPNPAG
                          625                         650                         675
VQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILSIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSG
                          700                         725                         750
ETVFMSMENPGLWILGCHNSDFRNRGMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNPPVLK
                          775                         800                         825
RHQREITRTTLQSDQEEIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLR
                          850                         875                         900
NRAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASRPYSFYSSLISYEE
                          925                         950                         975
DQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDVDLEKDVHSGLIGPLLVCHTNTLNPAHGR
                         1000                        1025                        1050
QVTVQEFALFFTIFDETKSWYFTENMERNCRAPCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYL
                         1075                        1100                        1125
LSMGSNENIHSIHFSGHVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSN
                         1150                        1175                        1200
KCQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMIIHGIKTQGARQKFS
                         1225                        1250                        1275
SLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFNPPIIARYIRLHPTHYSIRSTLRMELMGC
                         1300                        1325                        1350
DLNSCSMPLGMESKAISDAQITASSYFTNMFATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVT
                         1375                        1400                        1425
TQGVKSLLTSMYVKEFLISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIAL
          1438
RMEVLGCEAQDLY
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